REMARKS

STATUS OF THE CLAIMS

Claims 1-28 are pending in this application. Claim 1 has been amended. Following entry of the amendments claims 1-28 will be pending and at issue.

IDS

Applicant notes with appreciation the Examiner's thorough consideration of the references cited in the IDS (Form 1449) submitted on December 9, 2003, December 22, 2003, April 15, 2005, June 24, 2005, and February 5, 2007. The Examiner indicated that he did not consider the PCT Search Report, European Search Report, or the references listed thereon because the search reports are not information disclosure statements complying with 37 CFR 1.98. Applicant points out that all of the references listed on the PCT Search Report and European Search Report were listed on the latest or previous IDS's (Form 1449) and copies were attached. In the case of the European Search Report, the four patent references (one US and three PCT) were listed on Form 1449 and copies were included with that form that was submitted on February 5, 2007. The Office Action dated March 21, 2007 indicates that the Examiner considered those references. The two non-patent references listed on the European Search Report had already been on the first IDS Applicant submitted on December 15, 2003. Similarly, the references listed in the PCT Search Report were listed on the IDS submitted April 15, 2005 and copies were included. Applicant has provided to the Examiner the actual search reports merely to provide background as to why those search authorities found the references cited to be relevant.

SUPPORT FOR AMENDMENTS

The amendment adding footnote 1 to the specification is inherently supported by the tables appearing in the application as that footnote merely provides an aid to correlating the sequences in the tables to those appearing in the sequence listing. The remaining amendments to the specification are made to renumber the footnotes that follow footnote 1. Accordingly, the amendments to the specification add no new matter.

Claim 1 has been amended to add the limitation that the second reference set of expressed genes are "independent of the first reference set." Support for this limitation can be found throughout the specification as filed, including, e.g., at [00115].

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 1 was rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite because the Examiner stated that "it remain[s] unclear what the term 'direction' means." *See* Office Action p. 4. The Applicant disagrees with the Examiner that "direction" could be interpreted to be the "absolute value of differential expression." To one who is skilled in the art, the direction of gene expression is not a number, rather it is up or down; or over or under. Therefore it can have no absolute value. Paragraph [00160] of the Specification verifies this interpretation.

> Following these criteria, we identified 214 transcripts that are differentially expressed in the same *direction* in all five prostate cancer cell lines, relative to normal prostate epithelium (NPE), regardless of the presence or absence of serum (vs. 292 observed using data from high serum alone). 43 of these genes were consistently *up-regulated* and 171 were consistently *down-regulated* at least two-fold in all five cancer cell lines relative to NPE.

Claims 24-28 were rejected under 35 U.S.C. § 112, second paragraph as unclear because it is unclear which Seq ID No refers to which sequence listing when described as "assigned in order of appearance." Office Action p. 4. Applicant respectfully requests that the Examiner make the amendments shown above (starting on p. 2) to the substitute specification provided with the Response filed on December 21, 2006, as discussed in the interview of March 22, 2007 that is described below. Thus, Applicant respectfully requests withdrawal of these rejections.

INTERVIEW SUMMARY

In a telephone call on March 22, 2007 between Applicant's representatives, Antonia Sequeira, Michael Shuster, and the Examiner, the Examiner requested that the Applicant provide information regarding how the SEQ ID NOS added to the header of each Table in the substitute specification filed on December 21, 2006 correspond with the rows of the Tables. Applicant's representative confirmed with the Examiner that a footnote would be provided explaining the

correspondence and providing an example. This footnote is provided above in the section regarding Amendments to the Specification, starting on page 2.

REJECTIONS UNDER 35 U.S.C. § 103

Claims 1-23 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Backert et al. (Int. J. Cancer (1999) Volume 82, pages 868-874) in view of Bertucci et al. (Human Molecular Genetics (2000) Volume 9, Number 20, pages 2981-2991). Applicant traverses this ground of rejection.

Three requirements must be met for a prima facie case of obviousness. First, the prior art references must teach all the limitations of the claims. Second, there must be an apparent reason to modify the reference or combine the teachings to produce the claimed invention. Third, a reasonable expectation of success is required.

The cited prior art references do not teach all of the elements of the claims. The Examiner contends that the Backert et al. teaches "a first reference set of expressed genes," "a second reference set of expressed genes," "a concordance set of expressed genes" and a "subset of genes within said concordance set." Claim 1 has now been amended to point out more clearly that the first and second reference sets are independent of one another. Claim 1 now reads, in part,

"A method for identifying and recording a listing of a subset of genes, comprising:

identifying a first reference set of expressed genes, …

identifying a second reference set of expressed genes independent of the first reference set…"

The Examiner points only to page 870 of Backert as showing both first and second reference set of expressed genes as well as the concordance set and the subset of the concordance set. The Examiner points to page 870 as showing both the first sample (normal cells) and the second sample (carcinomatous cells), stating that Backert identifies genes that are differentially expressed, which the Examiner finds to be the first reference set. These experiments pointed to by the Examiner are the cDNA array experiments. The Examiner then indicates that Backert (at page 870) uses another set of samples that the Examiner finds to be the third sample (normal cells) and still another set that the Examiner finds to be the fourth sample (carcinomatous cells),

stating that these are used to find another set of genes that are the second reference set. These experiments pointed to by the Examiner are the Northern blot/RT-PCR experiments. The Examiner further seems to indicate that the 6 of the 10 alterations detected in the cDNA array that were confirmed by the Northern blot/RT-PCR experiments on page 870 are the concordance set, and the Examiner suggests that Backert's indication that the expression of 5 genes being lowered significantly (page 870) is the subset.

However, the experiments described on page 870 do not result in two reference sets that are independent of each other. The cDNA array as well as the Northern blot/RT-PCR experiments described are *both* performed on cells from same the three types of cell lines – normal, mucinous carcinomatous, and non-mucinous carcinomatous. The note at the bottom of Table II in Backert further confirms that the same cell lines were used for both the cDNA arrays and the Northern blot/RT-PCR experiments. Thus, at most, the experiments described on page 870 result in one reference set, not two. Backert fails to disclose identifiying a second reference set that is independent of the first reference set. Since there is no second reference set independent of the first, the experiments described on page 870 further cannot disclose a concordance set of those reference sets or a subset of a concordance set.

The Examiner further indicates that even if one reference set is used to verify another reference set, this is within the scope of the instant claims. Applicant respectfully disagrees. The claims include a step of identifying a first reference set and a step of identifying a second reference set. In the Examiner's analogy to Backert, a first reference set is identified via the cDNA array experiments through which Backert detects "10 alterations." Backert, p. 870. However, the Northern blot/RT-PCR experiments are simply done to verify those 10 alterations. There is no identification of a second reference set at all, much less an identification of a second reference set independent of the first. Backert simply takes the 10 previously identified genes and performs the Northern blot/RT-PCR experiments (see Table II illustrating this). He identifies no independent set. Under the Examiner's description above, the second reference set in Backert could only be the same 10 genes. In addition, there can be no identification of a concordance between these two sets that include the same 10 genes. The Examiner seemed to point to the 6 of 10 alterations that were confirmed by the Northern blot/RT-PCR experiments, but this is not a concordance set between two independent sets, but only a verification of a first set of 10 in which 6 were confirmed.

The Examiner then notes that Backet does teach that the first and second samples are independent of the third and fourth samples. However, in citing support for this, the Examiner points to the Applicant's discussion of page 871 of Backert in the prior Office Action Response. On page 871, Backert discloses further experiments involving human tissue. Backert explains at page 871 that he is testing the results obtained with the cell lines above (the cDNA array and Northern blot/RT-PCR) by performing other Northern blot/RT-PCR experiments involving tissue from 12 patients, which revealed altered expression of 2 genes. The Examiner cites this as support for his point that the third and fourth samples he indicated above must be independent from the first and second because the third and fourth samples are human tissue samples. However, these are not the same experiments pointed to above by the Examiner, so it is unclear as to why the Examiner believes this provides support for independent third and fourth samples being from human tissue. This seems to conflict with the Examiner's statement above that the cell lines from the Northern blot/RT-PCR experiments are the third and fourth samples. Even if the Examiner is now stating that these human tissue samples make up the third or fourth samples, again there is no second reference set because the same 10 alterations were examined. Further, there can be no concordance between the same two sets. Even if the Examiner found the 2 genes to be a concordance set, there is no subset of a concordance set between a reference set from the human tissue experiments and a reference set from the cell line experiments. Bertucci does not remedy this deficiency as Bertucci does not disclose identification of first and second reference sets as claimed.

The Examiner maintains that Bertucci teaches "a first correlation coefficient, correlating for said genes within said subset a first expression differential between said first and second samples to a second expression differential between third and fourth samples, exceeds a predetermined value." In the second full paragraph of the second column on page 2987 of Bertucci, it is reported that a correlation coefficient is used to verify experimental results and is used to measure reproducibility of differential expression between two samples that are the same. Bertucci does not disclose two reference sets, each derived from two samples that are of different phenotype. Even if, *arguendo*, the two samples in Bertucci are analogous to the two reference sets of the claimed invention, Bertucci's results that are being compared are from the same sample. However, in the claimed invention, the two references sets are independent of each other.

In sum, the correlation coefficient as claimed in the claimed invention serves as a measure of accuracy. The correlation coefficient as disclosed in Bertucci serves as a measure of precision. Therefore, Bertucci does not disclose a "a first correlation coefficient, correlating for said genes within said subset a first expression differential between said first and second samples to a second expression differential between third and fourth samples, exceeds a predetermined value."

Accordingly, the combination of Backert and Bertucci fails teach all of the elements of claim 1, and so cannot render independent claim 1 obvious, nor the claims that depend therefrom (claims 2-22). Therefore, withdrawal of this ground of rejection is respectfully requested.

Claims 12 and 13 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Backert et al. in view of Bertucci et al. and further in view of Young et al. (US Publication No. 2005/0255588 A1). Claims 12 and 13 depend from claim 10, which depends from claim 9, which depends from claim 1. Thus, claims 12 and 13 incorporate all of the elements of claim 1. Therefore, claims 12 and 13 cannot be rendered obvious by the cited art for at least the reasons described above regarding claim 1. Accordingly, Applicant requests withdrawal of this rejection of claims 12 and 13.

In conclusion, a *prima facie* case of obviousness has not been presented by the Office. Therefore, withdrawal of this ground of rejection of claims 1-22 is respectfully requested.

CONCLUSION

Withdrawal of the pending rejections and reconsideration of the claims are respectfully requested, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicant's representative at (650) 335-7185.

Respectfully Submitted,
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